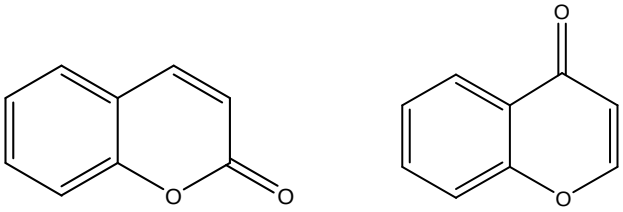
4.1 INTRODUCTION

The fusion of a pyrone ring with a benzene ring gives rise to a class of heterocyclic compounds known as benzopyrones, of which two distinct types are recognized (i) benzo-α-pyrones, commonly called coumarins, and (ii) benzo-γ-pyrones, called chromones, the latter differing from the former only in the position of the carbonyl group in the heterocyclic ring (Figure 4.1).



Benzo α- pyrone Benzo γ-pyrone

Figure 4.1 *Benzo pyrone structures*

Several coumarin derivatives have been found to be widely distributed in the plant kingdom, particularly the plants belonging to the natural orders of Orchidaceae, Leguminoceae, Rutaceae, Umbelliferae, and Labiatae that are rich sources of naturally occurring coumarins. Coumarin, the parent substance of the benzo-α-pyrone group, was first isolated from tonka beans in 1820.

Coumarins are an important group of organic compounds that are used as additives in food and cosmetics, optical brightening agents and dispersed fluorescent and laser dyes [1-3]. Many products which contain this subunit, exhibit useful and diverse biological activity such as molluscacides [4] that exhibit anthelmintic, hypnotic and insecticidal properties [5] or serve as anticoagulant agents [6] or fluorescent brighteners [7].

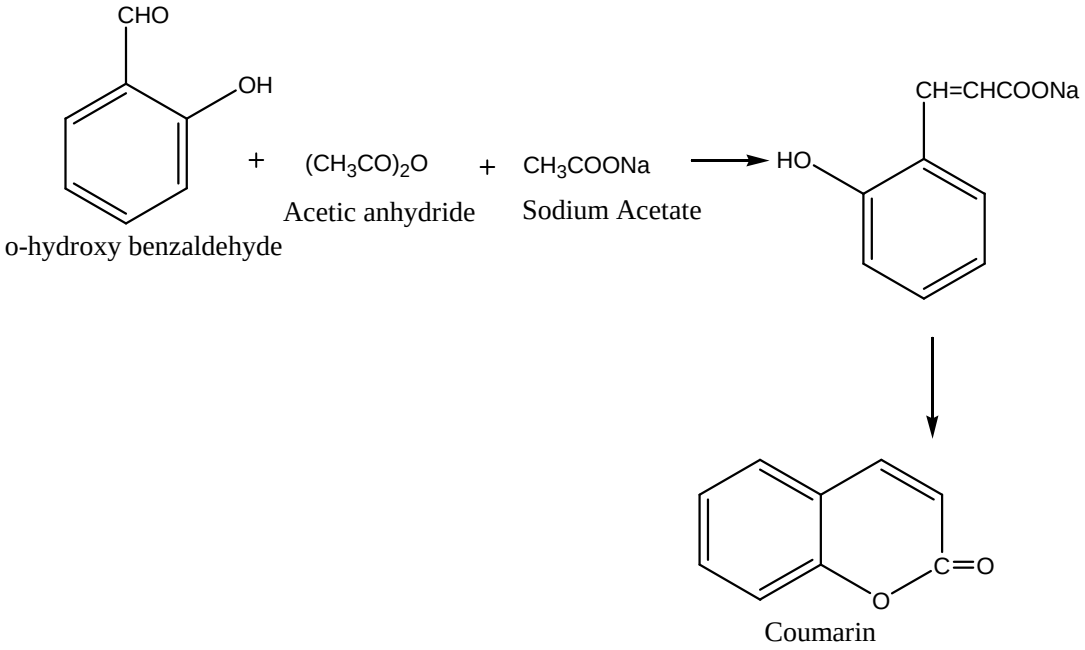
4.2 SYNTHETIC ROUTES TO COUMARINS

Various routes to coumarin synthesis [8] include the Pechmann [9], Perkin [10], Knoevenagel [11,12] and Reformatsky [13] reactions.

Perkin reaction

This classical method has entered into every textbook of organic chemistry. Perkin first synthesized coumarin from salicylaldehyde by heating it with acetic anhydride and anhydrous sodium acetate. This reaction occurs with the formation of an intermediate, o-hydroxycinnamic acid derivative, which passes spontaneously into the lactone, when dissociated from its sodium salt. This synthetic route has, however,

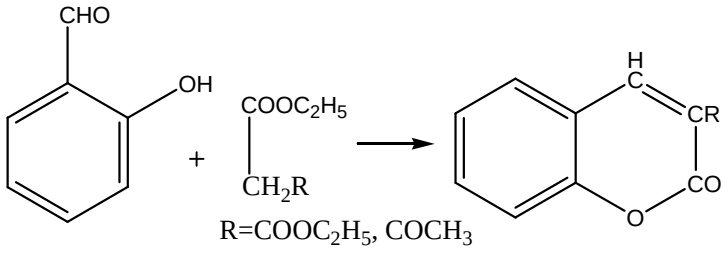
some limitations. It is rather difficult to obtain the appropriate initial o-hydroxy aldehydes in case of substituted phenols. Further, by this route, it is not possible to synthesise coumarins with substitution in pyrone ring. A schematic representation of Perkin reaction is given in Scheme 4.1.



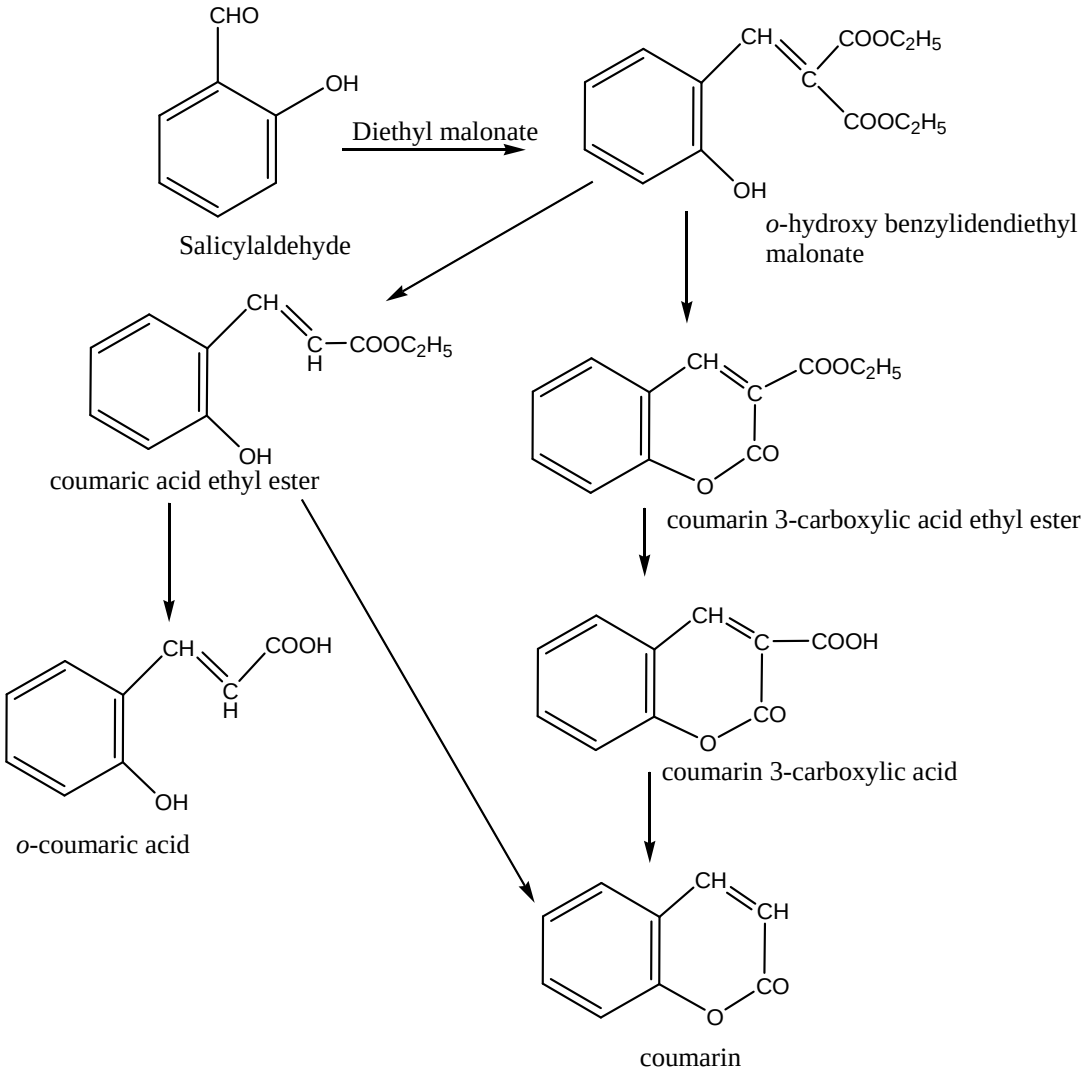
Scheme 4.1 *Perkin reaction*

Knoevenagel reaction

Knoevenagel developed a method for the synthesis of coumarin derivatives from o-hydroxyaldehydes by condensation with ethyl malonate, ethyl acetoacetate, ethyl cyanoacetate, etc., in the presence of piperidine, pyridine, and other organic bases (Scheme 4.2 and 4.3).



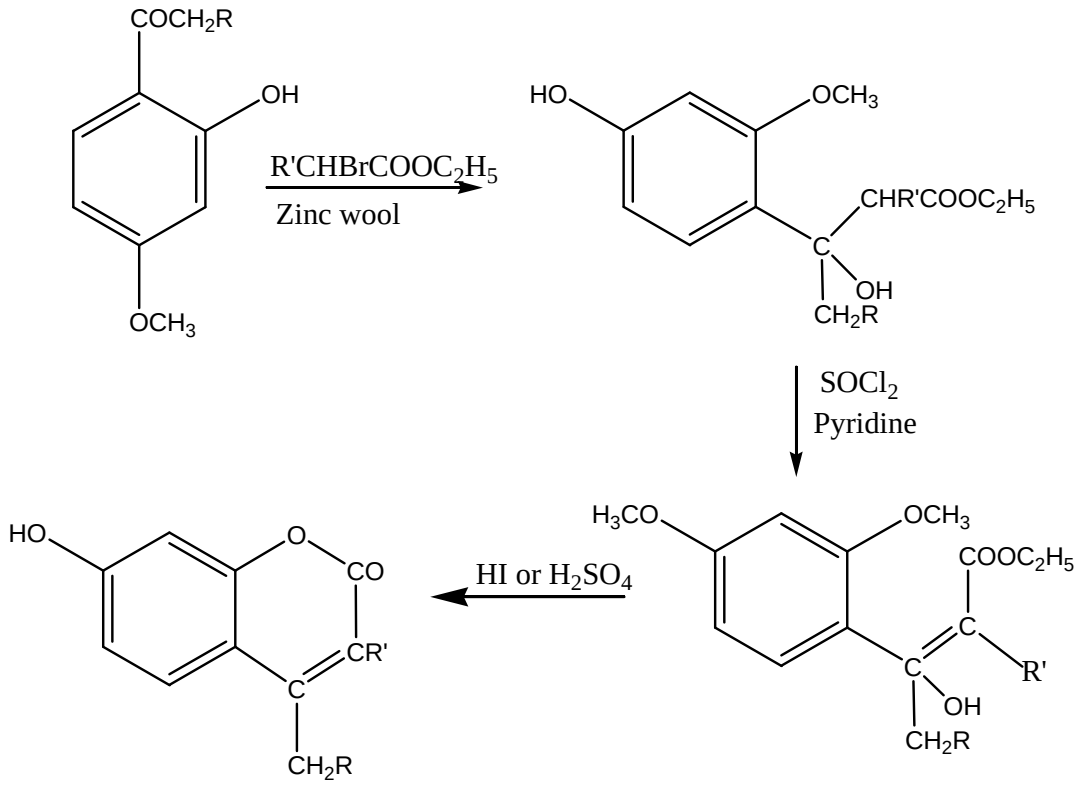
Scheme 4.2 *Knoevenagel reaction*



Scheme 4.3 *Reaction pathways for the synthesis of coumarin derivatives by Knoevenagel condensation* [14]

Reformatsky reaction

The Reformatsky reaction involves condensation of aldehydes (or ketones) with α-halo esters in presence of metallic zinc to form β-hydroxyesters. It was carried out by Sergei Nikolaevich Reformatsky. The Reformatsky reaction between α-haloester and a carbonyl compound constitutes one of the most useful methods for carbon-carbon bond formation in organic synthesis. 3,4-dialkyl-substituted coumarins not synthesised by the usual methods may be synthesized using Reformatsky reaction. *o*-hydroxy aryl/alkyl ketones, under the conditions of the Reformatsky reaction, are ultimately converted into coumarin derivatives. A reaction scheme for synthesis of coumarin by Reformatsky reaction is presented in Scheme 4.4.



Scheme 4.4 *Reformatsky Reaction*

Pechmann condensation

Pechmann condensation is the most widely applied method for coumarin synthesis, since it proceeds from simple starting materials i.e phenols and a β-keto ester, and gives good yields of coumarins with substitution in either the pyrone or benzene ring or in both. The course of the reaction depends on the substituents on the phenol, on the catalyst used and on the nature of the β-keto ester. Of the number of synthetic methods, there are a few which have yielded important results; there are several others whose applications are less general. All these methods center around the possibility of building up the pyrone ring on a suitable benzene derivative.

Conventionally, coumarins say 7-hydroxy-4-methylcoumarin can be obtained in high yields upon reaction of ethyl acetoacetate with 1,3 dihydroxybenzene (resorcinol) with sulphuric acid as solvent and condensing agent [15]. Aluminium chloride and trifluoroacetic acid [16] are also reported as condensing agents for synthesis of coumarins. Use of lewis acidic ionic liquid 1-butyl-3-methylimidazolium chloroaluminate is reported for coumarin syntheses via Pechmann condensation [17]. The reaction time is reduced drastically even at ambient conditions. The ionic liquid plays the dual role of solvent and Lewis acid catalyst providing a quick and efficient

route to the syntheses of coumarins. Kotharkar et al [18] have reported use of chlorosulfonic acid as an alternative to conventional acid catalysts in the Pechmann condensation.

The conventional process requires long reaction times, corrodes the reactor and creates by-products and salt waste due to neutralisation of the acid. As indicated earlier in Chapter 1, in view of the deficiencies encountered, there is a global effort to replace the conventional homogeneous liquid acid catalysts by heterogeneous solid acid catalysts. Therefore, attempts have been made to develop alternate, environmentally benign and heterogeneously catalyzed synthesis routes. The use of heterogeneous acid catalysts presents advantages, such as safer operating conditions, ease of product work up, reduced equipment corrosion, and minimized waste stream, combined with reusability of the catalyst.

4.3 LITERATURE SURVEY IN THE CURRENT AREA OF STUDY

Tyagi et al [19] have studied microwave (MW) assisted solvent free synthesis of hydroxy derivatives of 4-methyl coumarin using nano-crystalline sulfated-zirconia catalyst. The catalyst showed good activity for activated *m*-hydroxy phenol substrates, viz., phloroglucinol and pyrogallol with ethyl acetoacetate for the synthesis of 5,7-dihydroxy 4-methyl coumarin and 7,8-dihydroxy 4-methyl coumarin, respectively, showing significant yields ranging from 78 to 85% within 5–20 min at 130 °C. However, the less activated phenol and *m*-methyl phenol was observed to be inactive for the synthesis of 4-methyl coumarin and 4,7-dimethyl coumarin, respectively, under the studied experimental conditions. Benzylsulfonic acid functionalized zirconia based transition metal oxide mesoporous molecular sieves (Zr-TMS-BSA) [20] catalyst is reported as an alternative to conventional acid catalysts in the Pechmann condensation of aromatic alcohols with ethyl acetoacetate leading to the formation of coumarin derivatives in solvent free condition at 150 °C. Reddy et al [21] have reported a novel $SO_4^{2-}/Ce_xZr_{1-x}O_2$ catalyst for Pechmann condensation of phenols under solvent-free conditions. Jin et al have reported Pechmann condensation of phenols using SO_4^{2-}/ ZrO_2 and SO_4^{2-}/ TiO_2 solid super acids [22].

Singhal et al [23] have studied Pechmann condensation of phenols using MoO_3/Al_2O_3 catalysts under solvent free conditions and reported regeneration and reusability studies of the catalyst. Pechmann condensation of phenols have been

reported using Montmorillonite K10 and KSF as solid acid catalyst and toluene as solvent [24].

Pechmann condensation is reported using a metal complex bipyridine cobalt chloride as catalyst under solvent free conditions using conventional method as well as microwave irradiation. A faster reaction and higher yields compared to the conventional method and no side products were identified using microwave irradiation. Further, they have reported that, electron releasing groups on the phenol ring shows more reactivity and gives higher yields compared to simple phenol.

Patil et al [25] have reported ultrasound assisted Pechmann condensation of phenols with β-ketoesters to form coumarins, in the presence of Bismuth(III) Chloride catalyst at room temperature, with a considerable reduction of reaction time. Ultrasound was found to synergistically accelerate the condensation of phenol with β-ketoesters in the presence of $BiCl_3$. In the absence of ultrasound, under the same conditions, the reaction was found to be slow. Bahekar et al [26] have reported use of Samarium(III) nitrate hexahydrate as an alternative to conventional acid catalysts in the Pechmann condensation of phenols with ethyl acetoacetate leading to the formation of coumarin derivatives.

Maheshwara et al [27] have reported cost effective synthesis of coumarins via Pechmann condensation using heterogeneous recyclable catalyst ($HClO_4 \cdot SiO_2$) under solvent-free conditions.7-hydroxy-4-methylcoumarin, 7-methoxy-4-methylcoumarin and 7,8-benzo-4-methylcoumarin derivatives have been prepared using resorcinol, 3-methoxyphenol and 1-naphthol, respectively. The catalytic activity and the recycle studies of the catalyst in all the three reactions have been carried out and a probable mechanism for Pechmann condensation reported.

Torviso et al [28] have reported Pechmann condensation using Keggin heteropolycompounds as catalysts. The catalytic activity using several phenols such as resorcinol, 3,5-dimethoxyphenol, α-napthol and β-napthol were determined. High yield of product was obtained in the case of 4-methyl-7-hydroxycoumarin (80–95%), 4-methyl-5,7-dimethoxycoumarin (60–92%) and 4-methyl-7,8-benzocoumarin (90%). However, the 4-methyl-5,6-benzocoumarin yield was low. It was observed that the use of microwave radiation as power source increases the reaction yield and mainly decreases the reaction time. Sudha et al [29] have reported single step synthesis of 4-methyl 7-hydroxy coumarin over Al-MCM-41 and phosphotungstic acid supported

onto Al-MCM- 41 under solvent-free condition and observed that 20% heteropoly acid supported catalyst was the most active amongst all the catalysts studied.

Apart from the other heterogeneous catalysts, cation exchangers are emerging as attractive solid acid catalysts for Pechmann condensation of phenols. Synthesis of 7-hydroxycoumarins by Pechmann reaction using Nafion resin/silica nanocomposites as catalysts has been reported by Laufer et al [30] using toluene as solvent. 7-hydroxy-4-methylcoumarin was obtained in very high yields up to 81% over SAC containing 40% Nafion on silica (SAC 40) and 96% yield over SAC 80 (80% of Nafion in composite) in refluxing toluene after 2 h of contact time. In contrast to the reaction conditions of the Pechmann reaction in toluene, studied by van Bekkum and co-workers [31,32], the use of the Nafion resin/silica composite materials led to 50% reduction of catalyst amount and reaction time.

The synthesis of 7-hydroxy-4-methylcoumarin via the Pechmann reaction of resorcinol and ethyl acetoacetate over various Amberlyst-type catalysts using toluene as solvent has been investigated by Sabou et al [33]. The highest yield of 7-hydroxy-4-methylcoumarin was found over dry Amberlyst-S with 95% conversion and 98% selectivity in refluxing toluene after 2h of reaction time at 120^{o}C. Catalysts with fewer acid sites showed the best catalytic performance. However, these resins being polymers with organic framework exhibit limitation of thermal stability.

Hoefnagel et. al. have reported the use of Amberlyst – 15, H-Beta and Filtrol as solid acid catalysts for synthesis of coumarin derivatives via Pechmann condensation and observed that, these catalysts though require short reaction times, require high reaction temperature and solvent medium for removal of azeotropic water [34]. When Phosphotungstic acid was used, reaction time is short with good yields of coumarin, however the major disadvantage is that the catalyst cannot be regenerated and reused and requires the use of solvent [35]. Palaniappan et. al. have reported the use of polyaniline supported catalytic systems for synthesizing 7-hydroxy-4-methyl coumarin under solvent free conditions but with poor yields of coumarin [36]. Panda et. al. have reported mesoporous zirconium phosphate (m-ZrP) as a solid acid catalyst for the synthesis of coumarins via Pechmann condensation under conventional and microwave heating [37]. Makrandi et al have reported synthesis of coumarins via Pechmann condensation by grinding of different phenols and β-ketoesters in the presence of p-toluenesulfonic acid (p-TSA) at room

temperature under solvent free conditions [38]. Parhami et al have reported use of silica supported boric tri-sulfuric anhydride as a novel and efficient catalyst for solvent-free synthesis of coumarins *via* Pechmann condensation [39]. Sharma et al have reported a simple and highly efficient procedure for the synthesis of 2*H*-chromen-2-ones via Pechmann condensation, involving the grinding of different phenols and β -ketoesters in the presence of silica supported sulfuric acid at room temperature under solvent free conditions [40]. Datta et al have reported synthesis of coumarin derivatives using phosphotungstic acid intercalated Bentonite via pechmann condensation of phenols with ethyl acetoacetate using microwave irradiation [41].

From our laboratory, TMA salts have been reported as solid acid catalysts for synthesis of coumarin derivatives via Pechmann condensation of resorcinol, pyrogallol and phloroglucinol with methyl acetoacetate [42].

4.4 OBJECTIVES OF THE PRESENT WORK

In the present chapter, the potential utility of M(IV)PWs (Type-I Inherent SACs) and 12-TPA/M(IV)O_2 (Type-II Induced SACs) has been explored by studying Pechmann condensation as a model reaction, wherein phenols (resorcinol, pyrogallol, phloroglucinol, hydroquinone and p-nitrophenol) have been treated with methyl acetoacetate to give the corresponding coumarin derivatives under solvent free conditions using conventional and microwave (MW) heating. Reaction parameters, reaction time, reaction temperature, catalyst amount and mole ratio of the reactants have been optimized. Catalytic performance of Type-I and Type-II catalysts have been compared at optimized condition and correlated with acid properties of the materials. The performance ability of the catalysts have also been assessed for regenerated/ reactivated catalysts. A reaction mechanism has been proposed for solid acid catalyzed synthesis of coumarins via Pechmann condensation.

4.5 EXPERIMENTAL

Catalyst Synthesis and Characterization

The synthesis and characterization of Type-I catalysts ZrPW, TiPW, SnPW [Inherent SACs - M(IV)PWs] and Type – II catalysts 12-TPA/ZrO_2-20, 12-TPA/TiO_2-20, 12-TPA/SnO_2-20 [Induced SACs - 12-TPA/M(IV)O_2-20] have been discussed in Chapter 2.

Materials and Methods

Resorcinol, pyrogallol, phloroglucinol, hydroquinone, p-nitrophenol, methyl acetoacetate and ethyl acetate were procured from Merck (India). Reactions were performed under MW irradiation using microwave reactor, Milestone - Start Synth Microwave Synthesis Labstation and 250 watts MW power controlled via microprocessor in 1 watt increments. FTIR spectra of the synthesized coumarin derivatives were determined on Shimadzu (Model 8400S) using KBr pellet. EDX analysis for catalysts (fresh and spent) has been performed on Jeol JSM-5610-SLV scanning electron microscope.

Experimental setup

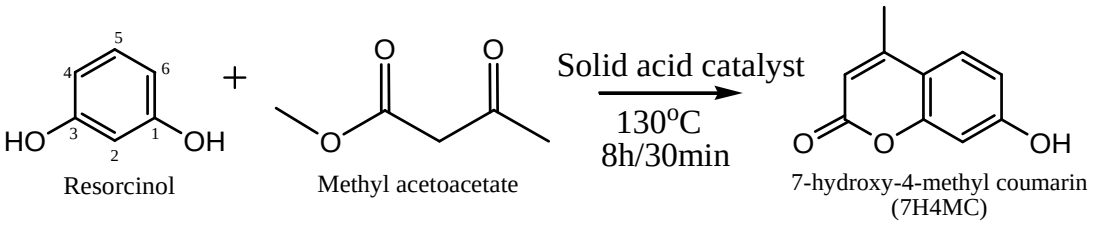
In a typical reaction, methyl acetoacetate (MA) (10-20 mmol) (substrate as well as solvent) and phenols (10-20 mmol) [resorcinol (R), pyrogallol (Py), phloroglucinol (Ph), hydroquinone (Hq) and p-nitrophenol (pNp)] was stirred with catalyst (0.10-0.25 g) in 50 ml two necked round bottom flask and refluxed for particular time (2-10 h) at particular temperature (120^oC-140^oC) under conventional heating. Reaction parameters reaction time, reaction temperature, catalyst amount and mole ratio of the reactants have been varied and conditions optimized. At optimized condition, the reactions were subjected to microwave (MW) irradiation (250W) for particular time (10-40 min).

After completion of reaction, the reaction mixture was cooled in an ice bath to obtain solid product, which was dissolved in ethyl acetate (2-5 ml), and catalyst was separated by filtration. The filtrate was distilled under vacuum, which yielded the crude product that was purified by recrystallization. All synthesized coumarin derivatives were characterized for IR spectroscopy and melting point. % yields were calculated on the basis of conversion of phenols.

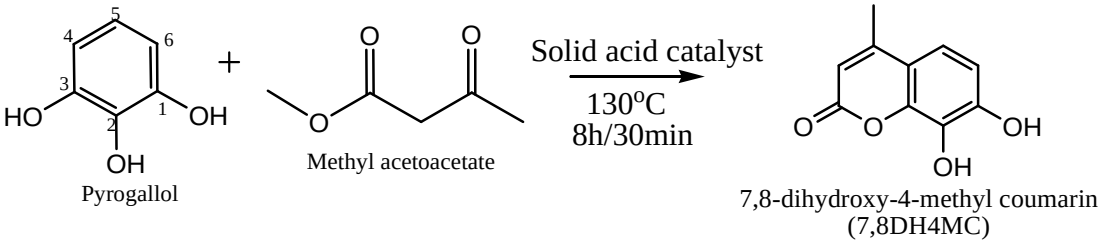
After separation of catalyst from reaction mixture by decantation/filtration, it is first refluxed in ethanol for 30 minutes to remove adsorbed molecules of reactants/products and then regenerated/reactivated as described in Chapter 3.

4.6 RESULTS AND DISCUSSION

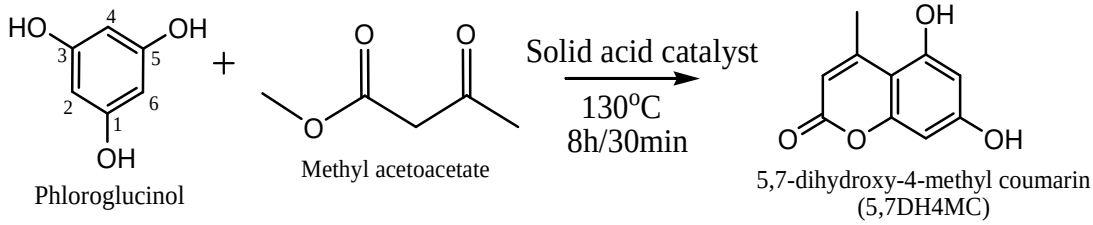
In the present study, Pechmann condensation of phenols (R, Py, Ph, Hq and pNp) with MA has been performed as described in experimental section. The Pechmann condensation of phenols with MA have been presented in schemes 4.5 – 4.9.



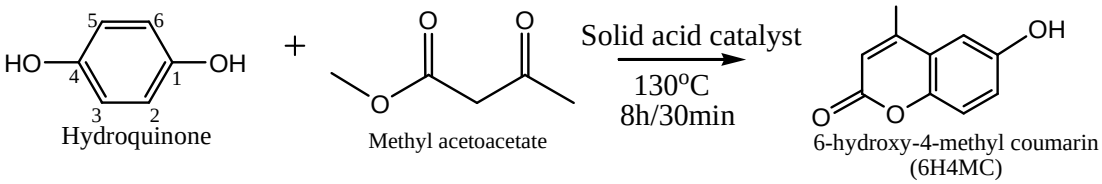
Scheme 4.5 *Synthesis of 7-hydroxy-4-methyl coumarin*



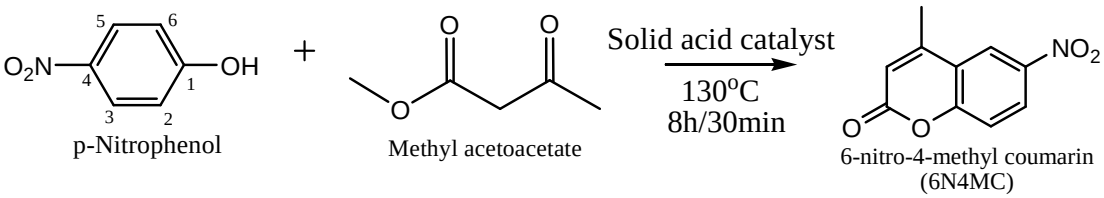
Scheme 4.6 *Synthesis of 7,8-dihydroxy-4-methyl coumarin*



Scheme 4.7 *Synthesis of 5,7-dihydroxy-4-methyl coumarin*



Scheme 4.8 *Synthesis of 6-hydroxy-4-methyl coumarin*



Scheme 4.9 *Synthesis of 6-nitro-4-methyl coumarin*

Firstly, reaction conditions were optimized using ZrPW and 12-TPA/ZrO_2-20 as solid acid catalysts for Pechmann condensation of R with MA (Table 4.1). For both the catalysts, it is observed that, yield increases with reaction time (2-10 h) until equilibrium is reached within 8 h (Figure 4.2). For the same reaction time, yield increased with increase in catalyst amount (0.10-0.25 g), attributed to increase in

number of active sites per g of substrate (Figure 4.3). Reactions were studied in the temperature range (120^oC-140^oC). A maximum product yield is obtained with reaction temperature 130^oC, beyond which product degradation is observed (Figure 4.4). Based on conditions optimized above by conventional heating, Pechmann condensation of resorcinol with methyl acetoacetate using ZrPW and 12-TPA/ZrO_2-20 as solid acid catalysts was now subjected to MW irradiation. It is observed that yield increased with increase in reaction time (10-40 min). Beyond 30 min, there is not much increase in % yield of coumarin derivative (Figure 4.5). Therefore, the reaction time was fixed to 30 min as optimum reaction time under MW irradiation.

At optimized conditions (Table 4.1; reaction time: 8 h under conventional heating and 30 min under MW heating; catalyst amount: 0.20 g; reaction temperature: 130^oC; mole ratio of R:MA – 1:1.5), Pechmann condensation of phenols (R, Py, Ph, Hq and pNp) with MA has been performed under conventional and MW heating using ZrPW, TiPW, SnPW, 12-TPA/ZrO_2-20 12-TPA/TiO_2-20 and 12-TPA/SnO_2-20 as solid acid catalysts to obtain products presented in scheme 4.5 - 4.9.

For all catalysts (Type – I and Type - II), order of % yield of coumarin derivatives obtained is 6H4MC > 5,7DH4MC > 7H4MC > 7,8DH4MC > 6N4MC. The substrate having electron – donating groups in the *para* position to the site of electrophilic substitution (for e.g. hydroquinone) gives higher yields [21]. Therefore, 6H4MC was obtained with high % yield. Comparing reactivity of hydroquinone and resorcinol, it is observed that during the formation of 6H4MC, electrophilic substitution can occur at both “2” or “6” and “3” or “5” positions simultaneously, in the hydroquinone moiety (Scheme 4.8). However, in the formation of 7H4MC, electrophilic substitution can occur only at “4 or 6” position of resorcinol moiety (scheme 4.5). The electrophilic substitution at “2” position in resorcinol cannot occur due to the steric hindrance of –OH group present at “3” and “1”. The reactivity of phloroglucinol was observed to be higher than pyrogallol, due to two hydroxyl groups at *meta*-positions in phloroglucinol compared to one hydroxyl group in pyrogallol [19]. This is due to the presence of three – OH groups (*meta* to each other) that cooperate in activating the aromatic ring for hydroxyalkylation. It is observed that, % yields of 7,8DH4MC are less than 7H4MC, attributed to steric hindrance of –OH groups present in pyrogallol (at “1”, “2” and “3” positions) compared to resorcinol (at

"1" and "2" positions) [21]. Low yield obtained in case of p-nitrophenol is attributed to the presence of electron withdrawing -NO_2 group in p-nitrophenol.

Pechmann condensation proceeds via acid-catalyzed reactions. Therefore, Pechmann reaction depends strongly on acidity of catalysts. Number and nature of surface acid sites play a predominant role in evaluating and correlating catalytic activity [42]. In the present study, amongst M(IV)PWs (Type - I catalysts) performance of catalyst is found to be TiPW > SnPW > ZrPW whereas, amongst 12-TPA/M(IV)O_2-20 (Type - II catalysts), the order is found to be 12-TPA/TiO_2-20 > 12-TPA/SnO_2-20 > 12-TPA/ZrO_2-20 which could be attributed to increased surface acidity of these materials (Table 2.5-2.10). Comparing performance of M(IV)PWs (Type - I catalysts) and 12-TPA/M(IV)O_2-20 (Type - II catalysts), M(IV)PWs scores over 12-TPA/M(IV)O_2-20 in terms of % yields/TON of coumarin derivatives formed (Table 4.2-4.11, Figure 4.7-4.16).

Higher yields/TON obtained under MW irradiation is probably due to the fact that the phenolic substrates and methyl acetoacetate being polar molecules, are microwave active and absorb the MW radiations rapidly and accelerate the rate of reaction. Formation of polar methanol (by-product) also helps in absorption of MW radiation thereby accelerating the reaction [19].

Regeneration/reactivation and reuse of catalysts

After each catalytic run, there is change in colour of the catalysts [pale yellow/light brown in case of 12-TPA/M(IV)O_2-20 and brown/red in case of M(IV)PWs]. This is probably due to the fact that reactant molecules come onto surface of catalyst and enter into reaction to give the product, while a few of them get adsorbed on surface. After each subsequent run, the acid sites were regenerated in case of type – I catalysts [M(IV)PWs] and reactivated in case of type – II catalysts [12-TPA/M(IV)O_2-20] as described in experimental section. All subsequent catalytic runs were performed at optimized conditions (Table 4.2 – 4.11).

It is observed that, on regeneration M(IV)PWs exhibited only a marginal decrease in % yields in each subsequent run, probably due to regeneration of the acid sites. However, a reactivation in case of 12-TPA/M(IV)O_2-20 exhibited a much higher decrease in % yields. In case of synthesis of 7H4MC, EDX analysis for both fresh and spent catalysts (ZrPW and 12-TPA/ZrO_2-20) has been performed after first catalytic run (Table 4.12; Figure 4.17 – 4.20). Decrease in atomic wt. % of Zr and W

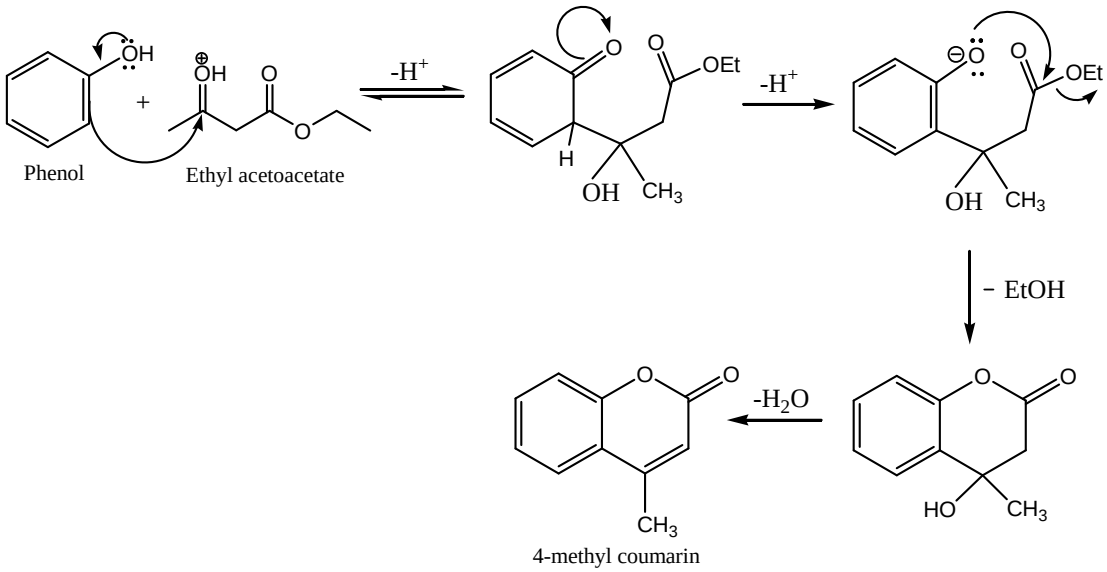
in ZrPW and 12-TPA/ZrO_2-20 is observed, indicating leaching of ions, which could be the probable reason for decrease in % yields.

When M(IV)PWs were used as such after each subsequent run (i.e. without regeneration), the decrease in % yields are much higher compared to regenerated M(IV)PWs, which is probably attributed to the deactivation of catalysts, due to substrate molecules getting adsorbed on surface or also entering interstices of the catalyst material [42].

Reaction mechanism for solid acid catalyzed Pechmann condensation

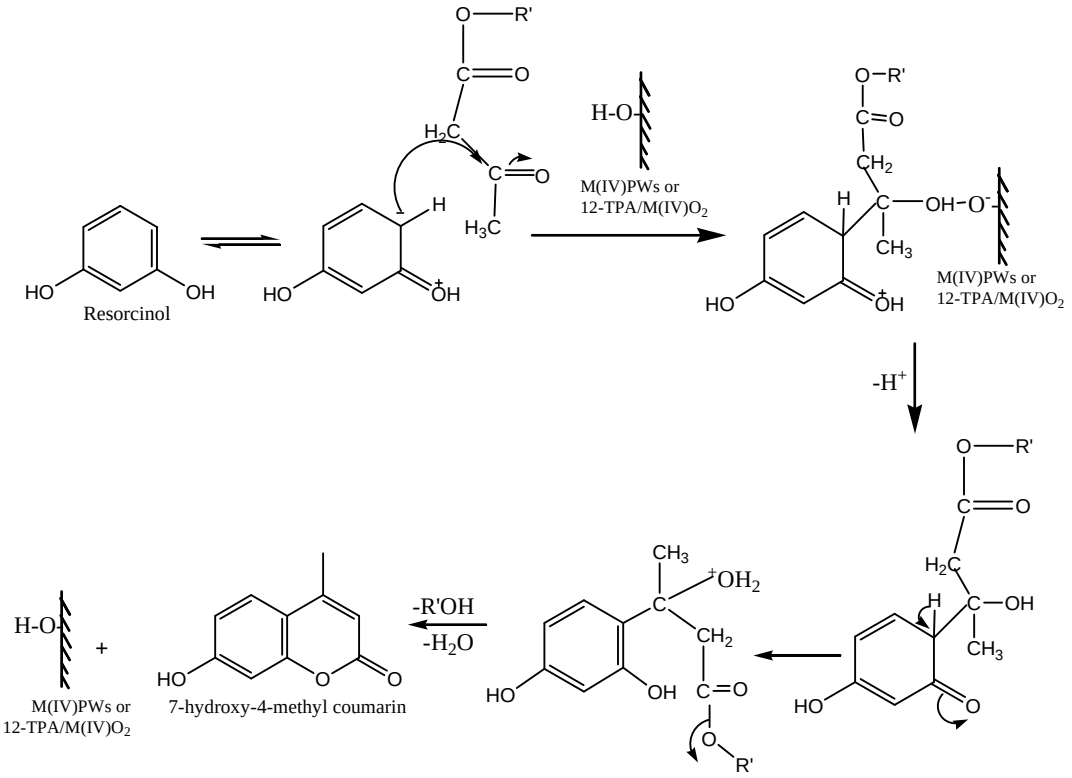
Conventional Pechmann reaction is conducted with a strong Brønsted acid such as methanesulfonic acid or a Lewis acid such as $AlCl_3$. The acid catalyses transesterification as well as keto-enol tautomerisation. A Michael Addition leads to the formation of the coumarin skeleton. A schematic of the reaction mechanism for Pechmann condensation is presented in Scheme 4.10.

This addition is followed by re-aromatization. Subsequent acid-induced elimination of water gives the product. The Pechmann condensation proceeds through transesterification followed by intramolecular hydroalkylation and dehydration [17,43,44]. These three steps are acid catalyzed reactions.



Scheme 4.10 *Mechanism for Pechmann condensation*

A possible mechanism for the Pechmann condensation of resorcinol and methyl acetoacetate using M(IV)PWs and 12-TPA/M(IV)O_2 is presented in scheme 4.11.



Scheme 4.11 *Proposed mechanism for the Pechmann condensation of phenols and β-ketoester using M(IV)PWs and 12-TPA/M(IV)O_2.*

Table 4.1 *Optimization of reaction conditions for Pechmann condensation of resorcinol (R) with methyl acetoacetate (MA) using ZrPW and 12-TPA/ZrO_2-20 under conventional and microwave (MW) heating.*

Set No.	Reactants	Mole ratio	Catalyst amount (g)	Reaction time (h/min)	Reaction temperature (^oC)	% Yield of 7H4MC	
						ZrPW	12-TPA/ ZrO_2-20
(A) Optimization of reaction time							
1	R+MA	1:1	0.10	2	130	4.88	No Product
2	R+MA	1:1	0.10	4	130	12.55	8.45
3	R+MA	1:1	0.10	6	130	28.31	19.65
4	R+MA	1:1	0.10	**8**	**130**	**43.90**	**37.55**
5	R+MA	1:1	0.10	10	130	44.62	38.00
(B) Optimization of reaction temperature							
6	R+MA	1:1	0.10	8	120	40.14	31.12
7	R+MA	1:1	0.10	8	140	39.83	28.56
(C) Optimization of catalyst amount							
8	R+MA	1:1	0.15	8	130	51.69	45.21
9	R+MA	1:1	**0.20**	8	130	**54.85**	**50.00**
10	R+MA	1:1	0.25	8	130	56.48	54.79
(D) Optimization of mole ratio of reactants							
11*	**R+MA**	**1:1.5**	**0.20**	**8**	**130**	**58.12**	**57.01**
12	R+MA	1:2	0.20	8	130	50.41	48.62
13	R+MA	1.5:1	0.20	8	130	51.47	49.00
14	R+MA	2:1	0.20	8	130	48.32	41.29
(E) Optimization of reaction time under MW irradiation							
15	R+MA[#]	1:1.5	0.20	10[#]	130	32.12	26.49
16	R+MA[#]	1:1.5	0.20	20[#]	130	49.83	44.00
17*	**R+MA[#]**	**1:1.5**	**0.20**	**30[#]**	**130**	**61.82**	**60.10**
18	R+MA[#]	1:1.5	0.20	40[#]	130	61.90	60.54

*([#]Reaction time in minutes under microwave heating; Yields refer to the isolated pure products; *****Optimum condition)*

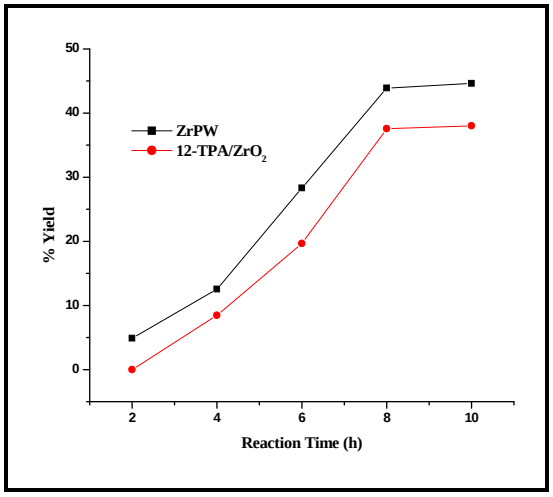


Figure 4.2 *Optimization of reaction time for synthesis of 7H4MC*

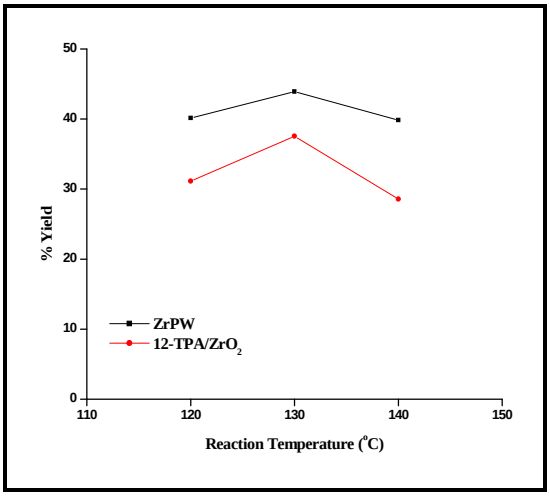


Figure 4.3 *Optimization of reaction temperature for synthesis of 7H4MC*

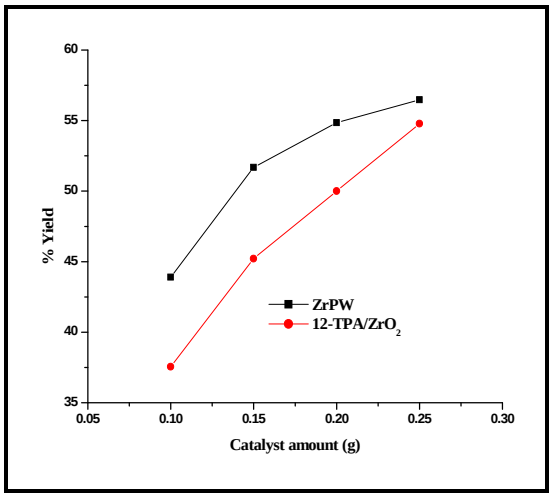


Figure 4.4 *Optimization of amount of catalyst for synthesis of 7H4MC*

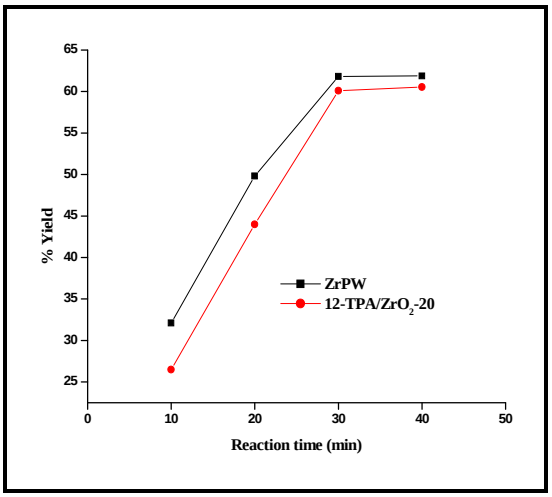


Figure 4.5 *Optimization of reaction time under MW irradiation for synthesis of 7H4MC*

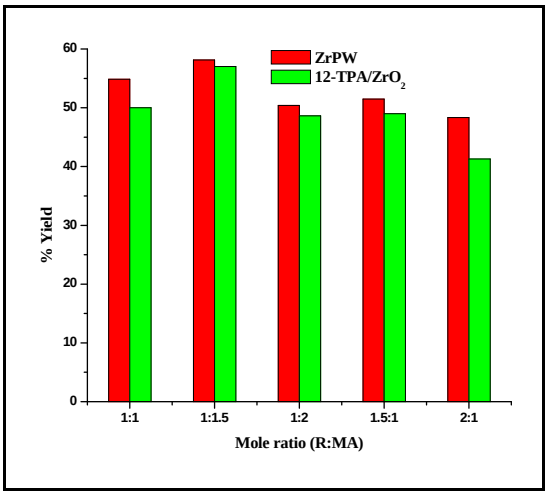


Figure 4.6 *Optimization of mole ratio of reactants for synthesis of 7H4MC*

Table 4.2 *Pechmann condensation of resorcinol (R) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under conventional heating.*

Catalyst	**% Yield (TON) of 7H4MC**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	58.12 (8.25) *(F)*	57.00 (8.09) *(Rg)*	55.39 (7.86) *(Rg)*
TiPW	69.37 (9.85) *(F)*	68.14 (9.67) *(Rg)*	65.10 (9.24) *(Rg)*
SnPW	62.48 (8.87) *(F)*	60.19 (8.54) *(Rg)*	58.40 (8.29) *(Rg)*
ZrPW	58.12 (8.25) *(F)*	49.32 (7.00) *(Ru)*	40.58 (5.76) *(Ru)*
TiPW	69.37 (9.85) *(F)*	61.78 (8.77) *(Ru)*	52.89 (7.51) *(Ru)*
SnPW	62.48 (8.87) *(F)*	54.33 (7.71) *(Ru)*	47.06 (6.68) *(Ru)*
12-TPA/ ZrO_2-20	57.01 (8.09) *(F)*	45.29 (6.43) *(Ra)*	34.19 (4.85) *(Ra)*
12-TPA/ TiO_2-20	58.00 (8.23) *(F)*	48.96 (6.95) *(Ra)*	39.47 (5.60) *(Ra)*
12-TPA/ SnO_2-20	57.50 (8.16) *(F)*	47.03 (6.67) *(Ra)*	35.00 (4.97) *(Ra)*

[Mole ratio of R:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 8h; F: Fresh catalyst; Rg: Regenerated catalyst; Ru: Reused catalyst (used as such, without regeneration); Ra: Reactivated catalyst; Yields refer to the isolated pure products]

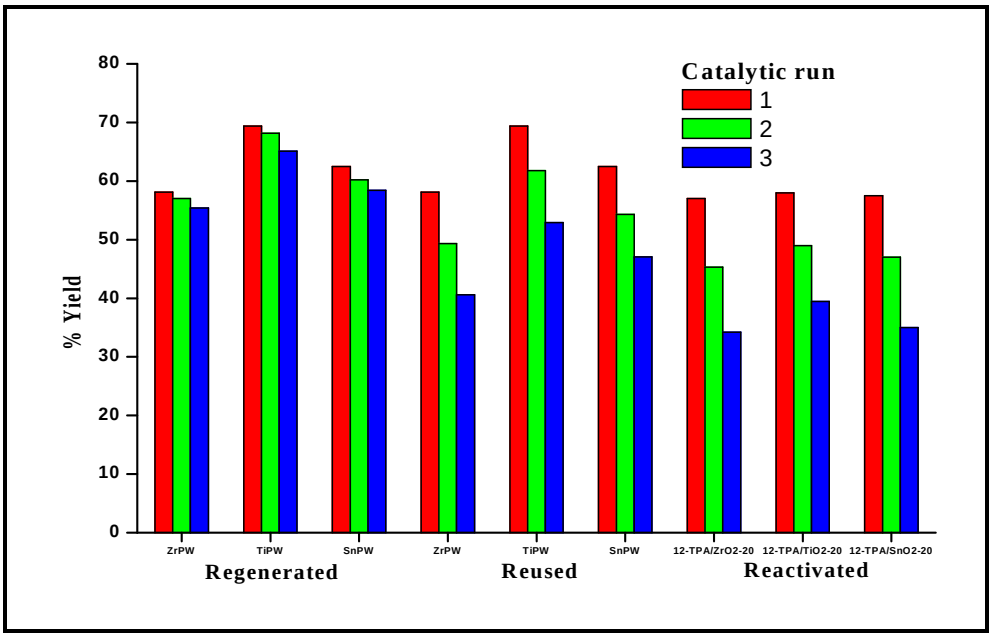


Figure 4.7 *Comparison of % yields of 7H4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under conventional heating.*

Table 4.3 *Pechmann condensation of resorcinol (R) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under microwave (MW) heating.*

Catalyst	**% Yield (TON) of 7H4MC**		
	Catalytic Run		
	1	***2***	***3***
ZrPW	61.82 (8.77) *(F)*	60.52 (8.59) *(Rg)*	57.89 (8.22) *(Rg)*
TiPW	71.83 (10.19) *(F)*	70.18 (9.96) *(Rg)*	67.18 (9.53) *(Rg)*
SnPW	64.18 (9.11) *(F)*	62.32 (8.84) *(Rg)*	61.90 (8.78) *(Rg)*
ZrPW	61.82 (8.77) *(F)*	53.11 (7.54) *(Ru)*	45.98 (6.52) *(Ru)*
TiPW	71.83 (10.19) *(F)*	63.43 (9.00) *(Ru)*	55.13 (7.82) *(Ru)*
SnPW	64.18 (9.11) *(F)*	56.09 (7.96) *(Ru)*	49.17 (6.98) *(Ru)*
12-TPA/ ZrO_2-20	56.10 (7.96) *(F)*	49.61 (7.04) *(Ra)*	34.22 (4.85) *(Ra)*
12-TPA/ TiO_2-20	60.94 (8.65) *(F)*	51.07 (7.25) *(Ra)*	41.38 (5.87) *(Ra)*
12-TPA/ SnO_2-20	58.87 (8.35) *(F)*	49.00 (6.95) *(Ra)*	39.21 (5.56) *(Ra)*

[Mole ratio of R:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 30 min.; F: Fresh catalyst; Rg: Regenerated catalyst; Ru: Reused catalyst (used as such, without acid treatment); Ra: Reactivated catalyst; Yields refer to the isolated pure products]

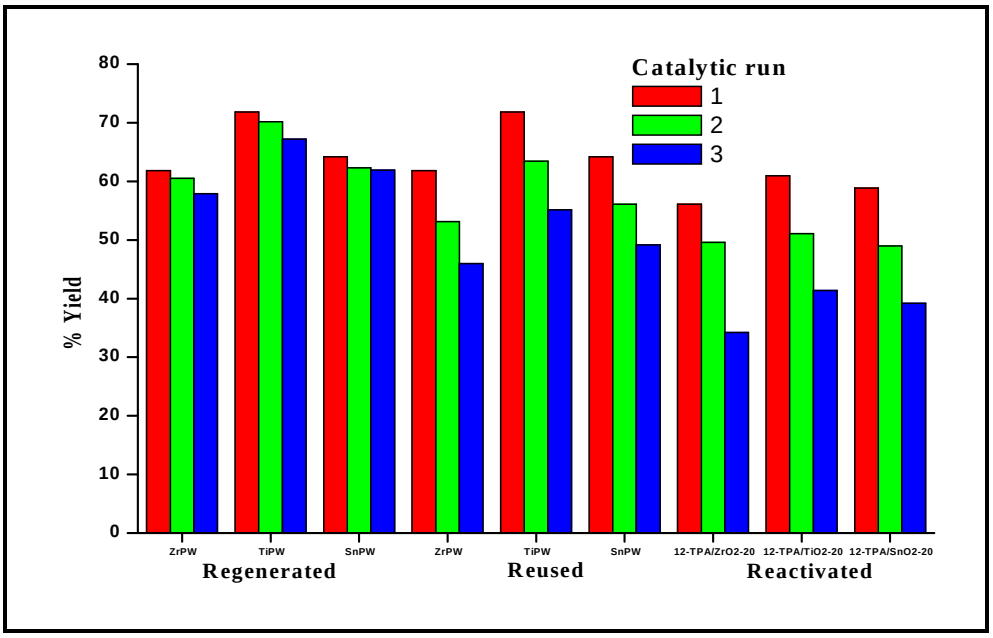


Figure 4.8 *Comparison of % yields of 7H4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under MW heating.*

Table 4.4 *Pechmann condensation of pyrogallol (Py) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under conventional heating.*

Catalyst	% Yield (TON) of 7,8DH4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	54.22 (8.13) *(F)*	52.00 (7.80) *(Rg)*	50.29 (7.54) *(Rg)*
TiPW	65.28 (9.79) *(F)*	64.57 (9.68) *(Rg)*	63.00 (9.45) *(Rg)*
SnPW	57.83 (8.67) *(F)*	56.00 (8.40) *(Rg)*	54.22 (8.13) *(Rg)*
12-TPA/ ZrO_2-20	48.45 (7.26) *(F)*	37.61 (5.64) *(Ra)*	25.49 (3.82) *(Ra)*
12-TPA/ TiO_2-20	52.60 (7.89) *(F)*	42.97 (6.44) *(Ra)*	32.64 (4.89) *(Ra)*
12-TPA/ SnO_2-20	50.72 (7.60) *(F)*	40.00 (6.00) *(Ra)*	31.77 (4.76) *(Ra)*

(Mole ratio of Py:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 8 h; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

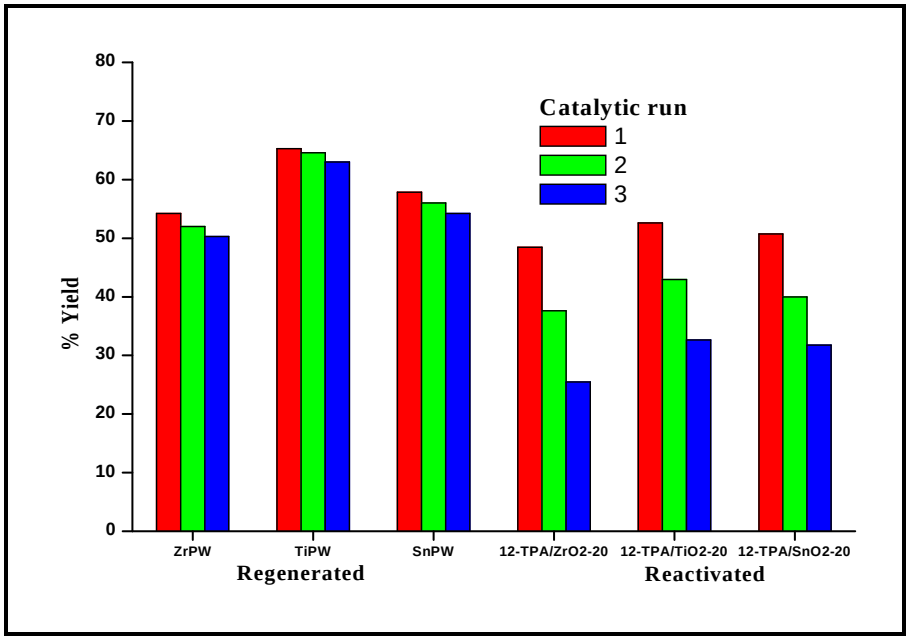


Figure 4.9 *Comparison of % yields of 7,8DH4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under conventional heating.*

Table 4.5 *Pechmann condensation of pyrogallol (Py) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under microwave (MW) heating.*

Catalyst	% Yield (TON) of 7,8DH4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	53.68 (8.05) *(F)*	51.45 (7.71) *(Rg)*	50.01 (7.50) *(Rg)*
TiPW	65.00 (9.75) *(F)*	63.98 (9.59) *(Rg)*	61.34 (9.20) *(Rg)*
SnPW	56.72 (8.50) *(F)*	54.89 (8.23) *(Rg)*	53.00 (7.95) *(Rg)*
12-TPA/ ZrO_2-20	49.82 (7.47) *(F)*	38.00 (5.70) *(Ra)*	27.98 (4.19) *(Ra)*
12-TPA/ TiO_2-20	53.00 (7.95) *(F)*	44.62 (6.69) *(Ra)*	34.50 (5.17) *(Ra)*
12-TPA/ SnO_2-20	51.37 (7.70) *(F)*	40.51 (6.07) *(Ra)*	29.67 (4.45) *(Ra)*

(Mole ratio of Py:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 30 min.; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

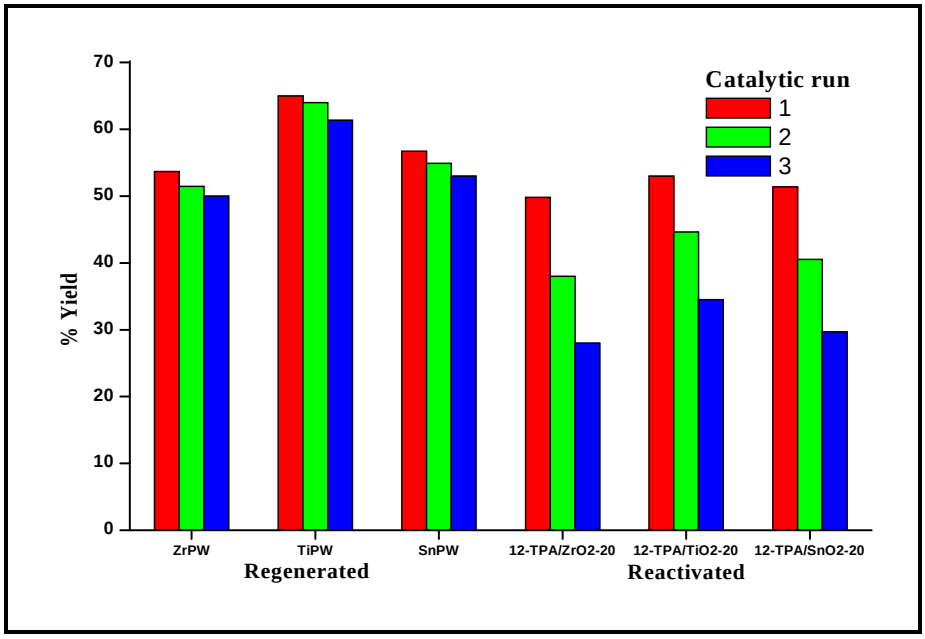


Figure 4.10 *Comparison of % yields of 7,8DH4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under MW heating.*

Table 4.6 *Pechmann condensation of phloroglucinol (Ph) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under conventional heating.*

Catalyst	% Yield (TON) of 5,7DH4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	61.00 (9.15) *(F)*	59.98 (8.99) *(Rg)*	58.00 (8.70) *(Rg)*
TiPW	76.82 (11.52) *(F)*	75.00 (11.25) *(Rg)*	73.65 (11.04) *(Rg)*
SnPW	63.89 (9.58) *(F)*	60.00 (9.00) *(Rg)*	58.19 (8.72) *(Rg)*
12-TPA/ ZrO_2-20	58.37 (8.75) *(F)*	46.22 (6.93) *(Ra)*	35.00 (5.25) *(Ra)*
12-TPA/ TiO_2-20	60.09 (9.01) *(F)*	49.30 (7.39) *(Ra)*	40.78 (6.11) *(Ra)*
12-TPA/ SnO_2-20	58.87 (8.83) *(F)*	48.07 (7.21) *(Ra)*	38.01 (5.70) *(Ra)*

(Mole ratio of Ph:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 8 h; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

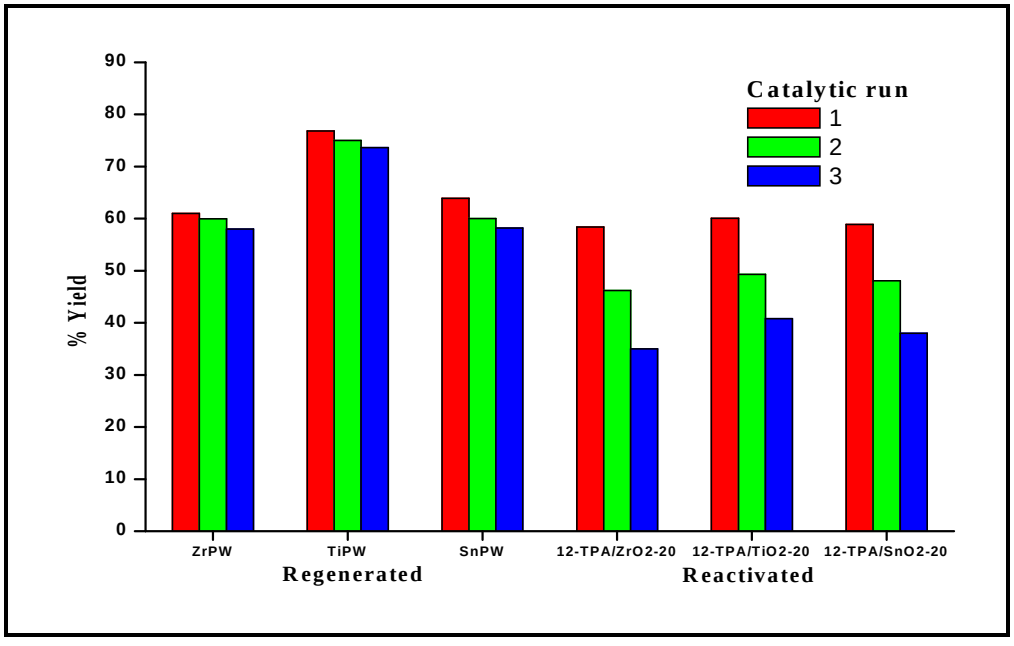


Figure 4.11 *Comparison of % yields of 5,7DH4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under conventional heating.*

Table 4.7 *Pechmann condensation of phloroglucinol (Ph) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under microwave (MW) heating.*

Catalyst	% Yield (TON) of 5,7DH4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	61.73 (9.25) *(F)*	60.19 (9.02) *(Rg)*	58.42 (8.76) *(Rg)*
TiPW	77.00 (11.55) *(F)*	75.82 (11.37) *(Rg)*	74.00 (11.10) *(Rg)*
SnPW	66.72 (10.00) *(F)*	64.08 (9.61) *(Rg)*	63.00 (9.45) *(Rg)*
12-TPA/ ZrO_2-20	60.19 (9.02) *(F)*	47.78 (7.16) *(Ra)*	36.12 (5.41) *(Ra)*
12-TPA/ TiO_2-20	61.00 (9.15) *(F)*	52.88 (7.93) *(Ra)*	43.94 (6.59) *(Ra)*
12-TPA/ SnO_2-20	60.32 (9.04) *(F)*	50.90 (7.63) *(Ra)*	40.11 (6.01) *(Ra)*

(Mole ratio of Ph:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 30 min.; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

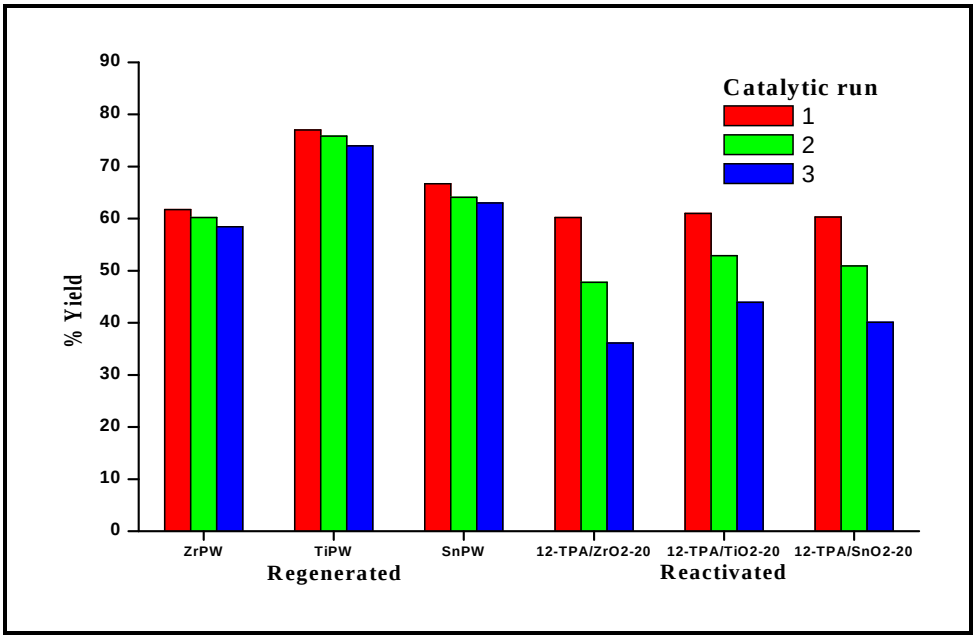


Figure 4.12 *Comparison of % yields of 5,7DH4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under MW heating.*

Table 4.8 *Pechmann condensation of hydroquinone (Hq) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under conventional heating.*

Catalyst	% Yield (TON) of 6H4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	64.48 (9.15) *(F)*	63.12 (8.96) *(Rg)*	60.18 (8.54) *(Rg)*
TiPW	78.18 (11.10) *(F)*	73.47 (10.43) *(Rg)*	72.54 (10.30) *(Rg)*
SnPW	70.18 (9.96) *(F)*	69.12 (9.81) *(Rg)*	67.42 (9.57) *(Rg)*
12-TPA/ ZrO_2-20	63.00 (8.94) *(F)*	48.10 (6.83) *(Ra)*	39.81 (5.65) *(Ra)*
12-TPA/ TiO_2-20	63.95 (9.08) *(F)*	57.63 (8.18) *(Ra)*	48.24 (6.85) *(Ra)*
12-TPA/ SnO_2-20	63.88 (9.07) *(F)*	50.08 (7.11) *(Ra)*	40.11 (5.69) *(Ra)*

(Mole ratio of Hq:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 8 h; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

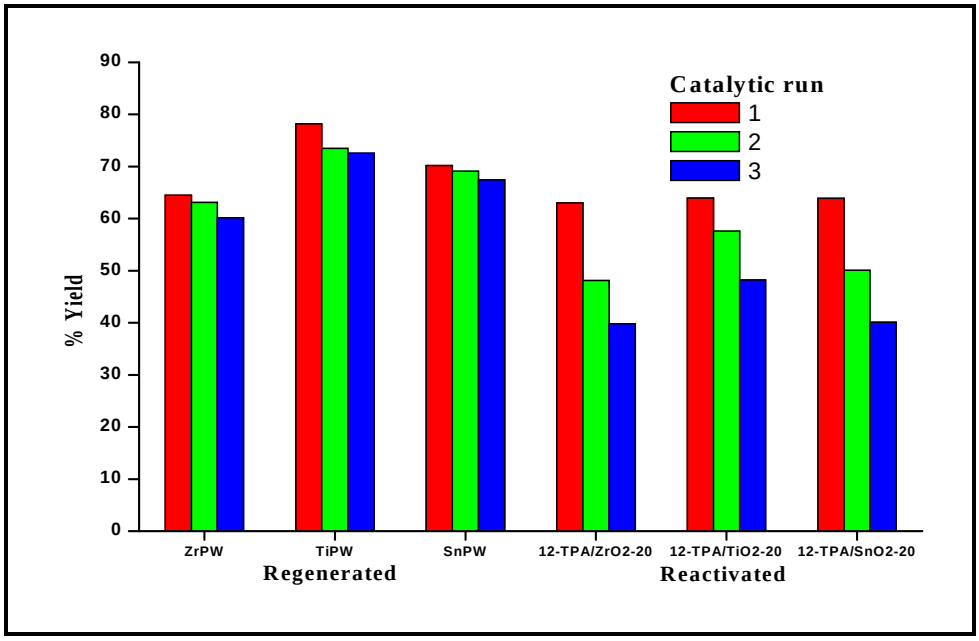


Figure 4.13 *Comparison of % yields of 6H4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under conventional heating.*

Table 4.9 *Pechmann condensation of hydroquinone (Hq) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under microwave (MW) heating.*

Catalyst	% Yield (TON) of 6H4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	66.37 (9.42) *(F)*	65.81 (9.34) *(Rg)*	62.31 (8.84) *(Rg)*
TiPW	79.88 (11.34) *(F)*	76.22 (10.82) *(Rg)*	74.00 (10.50) *(Rg)*
SnPW	72.88 (10.34) *(F)*	70.00 (9.94) *(Rg)*	67.51 (9.58) *(Rg)*
12-TPA/ ZrO_2-20	63.43 (9.00) *(F)*	47.12 (6.69) *(Ra)*	38.36 (5.44) *(Ra)*
12-TPA/ TiO_2-20	64.00 (9.08) *(F)*	61.19 (8.68) *(Ra)*	50.06 (7.10) *(Ra)*
12-TPA/ SnO_2-20	65.18 (9.25) *(F)*	51.30 (7.28) *(Ra)*	42.19 (5.99) *(Ra)*

(Mole ratio of Hq:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 30 min.; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

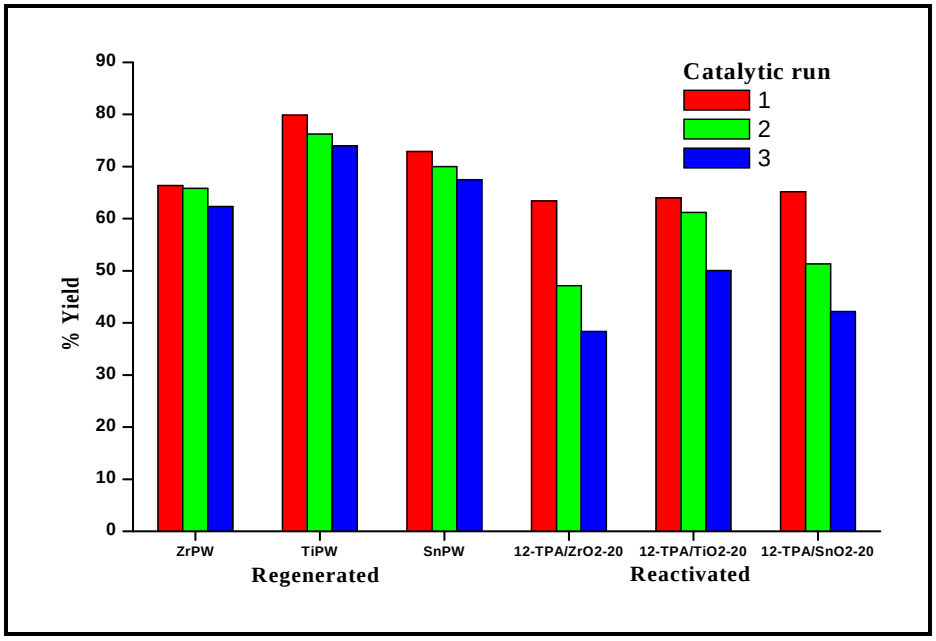


Figure 4.14 *Comparison of % yields of 6H4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under MW heating.*

Table 4.10 *Pechmann condensation of p-nitrophenol (pNp) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under conventional heating.*

Catalyst	% Yield (TON) of 6N4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	42.12 (6.59) *(F)*	41.00 (6.41) *(Rg)*	38.78 (6.06) *(Rg)*
TiPW	50.00 (7.82) *(F)*	48.28 (7.55) *(Rg)*	47.09 (7.36) *(Rg)*
SnPW	45.00 (7.04) *(F)*	43.44 (6.79) *(Rg)*	40.61 (6.35) *(Rg)*
12-TPA/ ZrO_2-20	38.18 (5.97) *(F)*	27.00 (4.22) *(Ra)*	17.56 (2.74) *(Ra)*
12-TPA/ TiO_2-20	41.87 (6.55) *(F)*	36.93 (5.77) *(Ra)*	25.86 (4.04) *(Ra)*
12-TPA/ SnO_2-20	40.21 (6.29) *(F)*	29.06 (4.54) *(Ra)*	20.11 (3.14) *(Ra)*

(Mole ratio of pNp:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 8 h; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

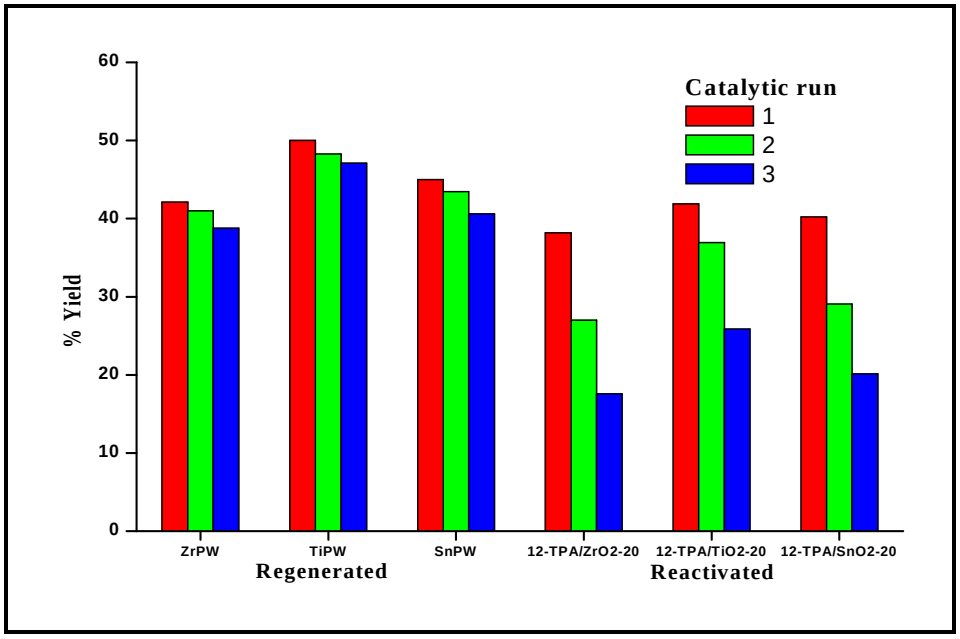


Figure 4.15 *Comparison of % yields of 6N4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under conventional heating.*

Table 4.11 *Pechmann condensation of p-Nitrophenol (pNp) with methyl acetoacetate (MA) using M(IV)PWs and 12-TPA/M(IV)O_2-20 at optimum condition under microwave (MW) heating.*

Catalyst	% Yield (TON) of 6N4MC		
	Catalytic Run		
	1	***2***	***3***
ZrPW	41.53 (6.49) *(F)*	39.89 (6.24) *(Rg)*	39.00 (6.10) *(Rg)*
TiPW	52.48 (8.21) *(F)*	51.00 (7.98) *(Rg)*	49.96 (7.81) *(Rg)*
SnPW	48.23 (7.54) *(F)*	42.71 (6.68) *(Rg)*	40.59 (6.35) *(Rg)*
12-TPA/ ZrO_2-20	38.68 (6.05) *(F)*	29.85 (4.67) *(Ra)*	18.00 (2.81) *(Ra)*
12-TPA/ TiO_2-20	41.92 (6.56) *(F)*	39.47 (6.17) *(Ra)*	28.04 (4.38) *(Ra)*
12-TPA/ SnO_2-20	40.99 (6.41) *(F)*	31.00 (4.85) *(Ra)*	19.99 (3.12) *(Ra)*

(Mole ratio of pNp:MA-1:1.5; Catalyst amount: 0.2g; Reaction temperature: 130°C; Reaction Time: 30 min.; F: Fresh catalyst; Rg: Regenerated catalyst; Ra: Reactivated catalyst; Yields refer to the isolated pure products)

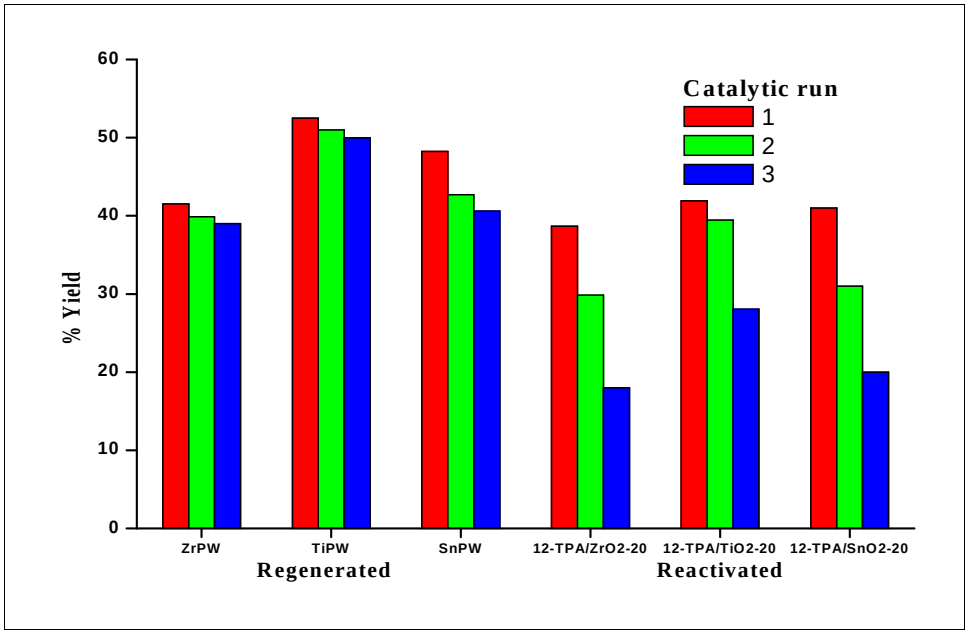


Figure 4.16 *Comparison of % yields of 6N4MC at optimized condition using M(IV)PWs and 12-TPA/M(IV)O_2-20 under MW heating.*

Table 4.12 *Elemental analysis by EDX for both fresh and spent ZrPW and 12-TPA/ZrO_2-20 in the synthesis of 7H4MC.*

Reactants	Materials	% by EDX analysis			
		Zr	**P**	**W**	**O**
R+MA	ZrPW (Fresh)	60.79	18.53	20.67	-
	ZrPW (Spent)	54.26	25.55	20.19	-
	12-TPA/ZrO_2-20 (Fresh)	28.75	0.11	3.44	67.70
	12-TPA/ZrO_2-20 (Spent)	26.12	0.54	2.81	70.53

(Mole ratio of R:MA -1:1.5; Catalyst amount -0.2g; Reaction temperature -130°C; Reaction Time: 8h)

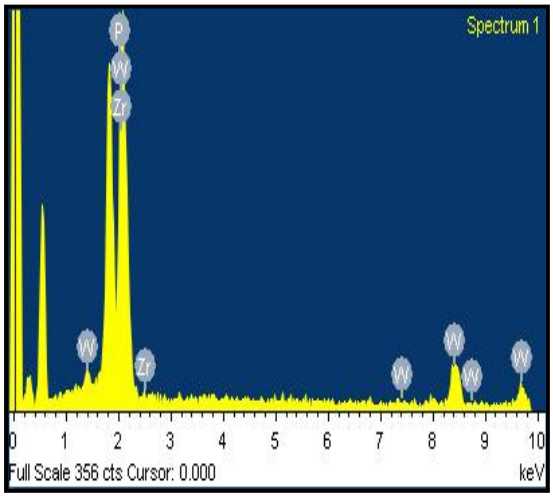


Figure 4.17 *EDX of fresh ZrPW*

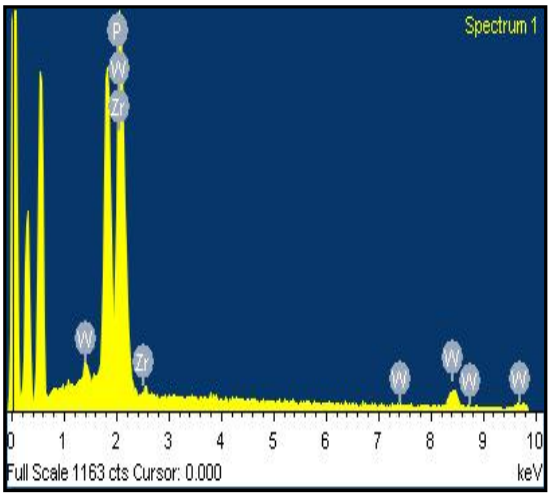


Figure 4.18 *EDX of spent ZrPW for synthesis of 7H4MC*

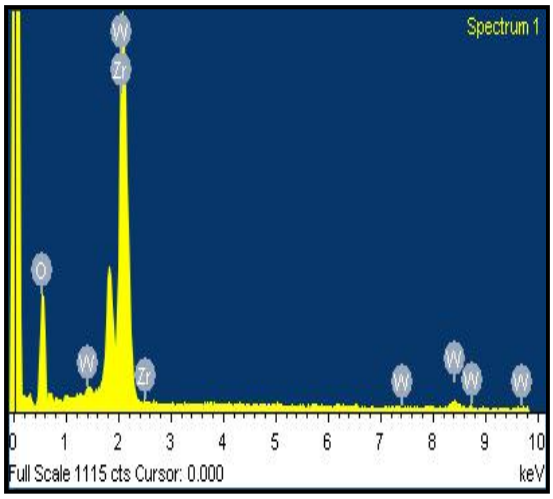


Figure 4.19 *EDX of fresh 12-TPA/ZrO_2-20*

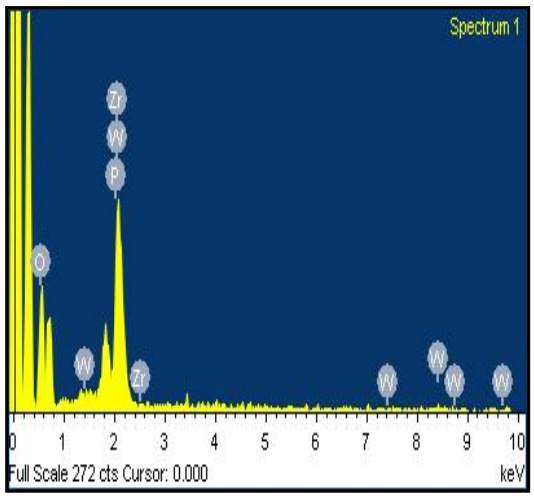
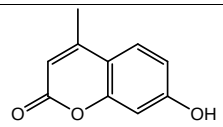
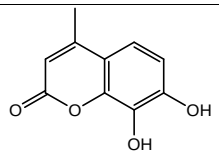
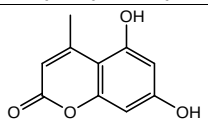
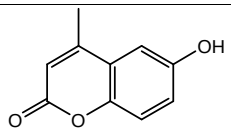
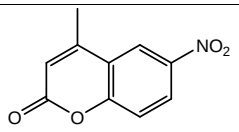


Figure 4.20 *EDX of spent 12-TPA/ZrO_2-20 for synthesis of 7H4MC*

Characterization of the products

The isolated products were characterized by melting point and FTIR spectroscopy (Table 4.13). Melting points are in good agreement with reported values [35].

Table 4.13 *Characterization of coumarin derivatives.*

Product formed	M.P. (^oC)	Bands observed in FTIR spectrum
 7-hydroxy-4-methyl coumarin	185-186	3155 cm^{-1}, 1678 cm^{-1}, 1227 cm^{-1}, 1057 cm^{-1}, 974 cm^{-1}, 844 cm^{-1}, 748 cm^{-1}.
 7,8-dihydroxy-4-methyl coumarin	244-245	3420 cm^{-1}, 1839 cm^{-1}, 1597 cm^{-1}, 1447 cm^{-1}, 1325 cm^{-1}, 1270 cm^{-1}, 1061 cm^{-1}, 901 cm^{-1}, 784 cm^{-1}, 515 cm^{-1}.
 5,7-dihydroxy-4-methyl coumarin	283-284	3447 cm^{-1}, 1865 cm^{-1}, 1660 cm^{-1}, 1618 cm^{-1}, 1530 cm^{-1}, 1456 cm^{-1}, 1160 cm^{-1}, 815 cm^{-1}, 750 cm^{-1}, 570 cm^{-1}
 6-hydroxy-4-methyl coumarin	165-166	3200 cm^{-1}, 1820 cm^{-1}, 1597 cm^{-1}, 1447 cm^{-1}, 1053 cm^{-1}, 832 cm^{-1}, 725 cm^{-1}, 575cm^{-1}.
 6-nitro-4-methyl coumarin	149-150	2920 cm^{-1}, 1788 cm^{-1}, 1567 cm^{-1}, 1440 cm^{-1}, 1325 cm^{-1}, 1250 cm^{-1}, 1061 cm^{-1}, 922 cm^{-1}, 854 cm^{-1}, 795 cm^{-1}.

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